Amendments to the Drawings:

The attached drawing sheet includes changes to Fig. 1. This sheet replaces the original sheet which includes Fig. 1.

Attachment: Replacement Sheet

REMARKS

The Office Action and the cited and applied references have been carefully reviewed. No claim is allowed. Claims 1-15 and 23-41 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

The disclosure has been objected to because there appears to be a typographical error in the sequence listing for SEQ ID NO:1, an amino acid sequence surrounding the β-secretase cleavage site on AβPP, in which amino acid residues 22 and 23 appear to be switched. The examiner notes that the sequence for AβPP is well recognized in the art and the art specifies these residues as Lys22 and Leu23. Appropriate correction is made to the sequence listing as required by the examiner, thereby obviating this objection. A proposed correction to the drawing to correct the same typographical error is attached hereto for the examiner's approval.

The examiner indicates that this application fails to comply with the requirements of 37 CFR §§1.821-1.825 because the disclosure contains sequences that need sequence identifier numbers, i.e., paragraph [00134] on page 49. Appropriate correction is made to the specification.

Applicants have added into the present specification a substitute paper copy Sequence Listing section according to 37 C.F.R. §1.821(c). Furthermore, attached hereto is a file (either on a 3½" disk or in an online text file) containing the "Sequence Listing" in computer readable form in accordance with 37 C.F.R. §1.821(e).

Applicants have amended the specification to insert SEQ ID Nos, as supported in the present specification.

The following statement is provided to meet the requirements of 37 C.F.R. §1.825(a) and 1.825(b).

I hereby state, in accordance with 37 C.F.R. §1.825(a), that the amendments included in the substitute sheets of the sequence listing are believed to be supported in the application as filed and that the substitute sheets of the sequence listing are not believed to include new matter.

I hereby further state, in accordance with 37 C.F.R. §1.825(b), that the attached copy of the computer readable form is the same as the attached substitute paper copy of the sequence listing.

Under U.S. rules, each sequence must be classified in <213> as an "Artificial Sequence", a sequence of "Unknown" origin, or a sequence originating in a particular organism, identified by its scientific name.

Neither the rules nor the MPEP clarify the nature of the relationship which must exist between a listed sequence and an organism for that organism to be identified as the origin of the sequence under <213>.

Hence, counsel may choose to identify a listed sequence as associated with a particular organism even though that sequence does not occur in nature by itself in that organism (it may be, e.g., an epitopic fragment of a naturally occurring protein, or a cDNA of a naturally occurring mRNA, or even a substitution mutant of a naturally occurring sequence). Hence, the identification of an organism in <213> should not be construed as an admission that the sequence *per se* occurs in nature in said organism.

Similarly, designation of a sequence as "artificial" should not be construed as a representation that the sequence has no association with any organism. For example, a primer or probe may be designated as "artificial" even though it is necessarily complementary to some target sequence, which may occur in nature. Or an "artificial" sequence may be a substitution mutant of a natural sequence, or a chimera of two or more natural sequences, or a cDNA (i.e., intron-free sequence) corresponding to an intron-containing gene, or otherwise a fragment of a natural sequence.

The examiner should be able to judge the relationship of the enumerated sequences to natural sequences by giving full consideration to the specification, the art cited therein, any further art cited in an IDS, and the results of his or her sequence search against a database containing known natural sequences.

Claims 1-3, 5-10, and 15 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 6, 10, 16-17 and 21-24 of copending application no. 10/481,642. This rejection is respectfully traversed.

The claims of copending application 10/481,642 are directed to an antigenic product carrying an antigenic peptide that comprises an epitope of a deposit-forming polypeptide involved in a plaque-forming disease or disorder. The deposit-forming polypeptide is recited in claim 5 as amyloid β and the epitope is recited in claims 6 and 7 as comprising the amino acid sequence of either SEQ ID NO:5 or SEQ ID NO:1, both of which contain the sequence EFRH but not the β-secretase cleavage site (e.g., the intact β-secretase cleavage site is not present in amyloid β). Moreover, AβPP (APP) as the precursor protein is not a deposit-forming polypeptide as it itself does not form a deposit. Accordingly, the instant claims directed to an immunizing composition comprising an

antigenic product which induces an immune response against the β-secretase cleavage site of AβPP are not obvious over claims to an antigenic product comprising an epitope that only appears in amyloid β, a product of β-secretase cleavage of AβPP. Newly added claims 23-41, which recite specific β-secretase cleavage site epitopes, also are not obvious over the claims of copending application 10/481,642.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 11 and 14 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10 and 11 of copending application 11/45,247. Application 11/475,247 has already been abandoned and therefore this rejection is moot.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 11, 12 and 14 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3 and 10 of copending application 11/073,526. This rejection is respectfully traversed.

The claims of copending application 11/073,526 requires that the displayed polypeptide comprises at least one epitope of β-amyloid. However, as argued above with regard to

the obviousness-type double patenting rejection over application 10/481,642, an epitope of β-amyloid (amyloid β or Aβ) does not contain the β-secretase cleavage site of AβPP and therefore would not induce an immune response against the β-secretase cleavage site of AβPP as required by the instant claims. Accordingly, instant claims 11, 12 and 14 along with newly added claims 23-41 are not made obvious by the claims of copending application 11/073,526.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 1 and 15 have been rejected under 35 U.S.C. §102(e) as being anticipated by WO01/53457 (Srivastava) as evidenced by Vassar et al., *Science* 286:735-741 (1999). The examiner states that Srivastava teaches that peptide fragments of a mutant APP comprising a mutation of codon 670 or 671, corresponding to the Swedish-type mutation, may be used as antigenic peptides. This rejection is respectfully traversed.

While Srivastava discloses a mutation at codon 671 (P2) or codon 672 (P1) of AβPP (APP), there is no disclosure that the antigenic peptide induces an immune response against the β-secretase cleavage site as recited in instant claim 1 or comprises an AβPP epitope <u>spanning</u> the β-secretase cleavage site as recited in new claim 23. Certainly, there can be

antigenic peptides of a mutant AβPP which may contain a mutation at codon 670 or 671 but not contain an epitope that spans the β-secretase cleavage site. Therefore, such antigenic peptides would not induce an immune response against the β-secretase cleavage site. The Board decision in *Ex Parte Cyba*, 155 USPQ 757, which held that "In order that a rejection based upon inherency may be sustained such inherency must be certain" (emphasis added), would apply here. Accordingly, Srivastava does not anticipate the present claims.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claim 1 has been rejected under 35 U.S.C. §102(b) as being anticipated by US Patent 5,721,130 (Seubert et al.). This rejection is respectfully traversed.

Seubert teaches at column 5, lines 20-24:

> The novel secreted fragments comprise the amino-terminal portion of βAPP which remains after such cleavage and will be referred to hereinafter as the amino-terminal fragment form of βAPP (ATF-βAPP).

and at column 6, lines 54-59:

> One suitable synthetic peptide consists of six residues of ATF-βAPP (ISEVKM) (SEQ ID NO:3) which are located on the immediate amino-terminal side of βAP…

Thus, it is clear that ATF-βAPP, like βAP (β-amyloid), is a β-secretase cleavage product of AβPP and therefore cannot

contain the intact β-secretase cleavage site. Accordingly, Seubert cannot anticipate the present claims which requires that the antigenic product induce an immune against the β-secretase cleavage site of AβPP (βAPP). New claim 23 further requires that the antigenic product comprises at least one epitope spanning the β-secretase cleavage site of AβPP, a requirement that is clearly not met by Seubert.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 1-11 and 13-15 have been rejected under 35 U.S.C. §102(b) as being anticipated by WO 00/72880 (Schenk et al.). The examiner states that Schenk teaches an immunizing composition comprising a fusion polypeptide, designated as pBx6, containing APP amino acid residues 592-695, and an adjuvant and used to immunize PDAPP transgenic mice. It is the examiner's position that, because residues 670/671 of APP are noted to be <u>proximate</u> to the β-secretase cleavage site, the APP polypeptide taught by Schenk containing residues 592-695 would comprise the β-secretase cleavage site of APP as well as instant SEQ ID NO:5 and residues 1-8 of instant SEQ ID NO:1. The examiner further asserted that the PDAPP mice would meet the limitation of "a subject in need thereof" recited in the immunization method of instant claim 15. This rejection is respectfully traversed.

Claim 15 is amended to recite "a human subject in need thereof", thereby obviating the rejection insofar as claim 15 is concerned.

Regarding claims 1-11, 13 and 14, the APP polypeptide containing residues 592-695 is 104 residues long and would therefore contain many epitopes besides an epitope spanning the β-secretase cleavage site. There is certainly no disclosure in Schenk of the specific epitopes spanning the β-secretase cleavage site in AβPP as recited in new claim 23 and there is no certainty of inducing an immune response against the β-secretase cleavage site of AβPP as recited in claim 1. The Board decision in *Ex Parte Cyba*, 155 USPQ 757 holding that "In order that a rejection based upon inherency may be sustained such inherency must be certain" (emphasis added) is also applicable in this rejection. Accordingly, Schenck does not anticipate the presently claimed invention.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 11 and 12 have been rejected under 35 U.S.C. §103(a) as being unpatentable over WO 00/72880 (Schenk et al.) in view of Frenkel et al., *Proc. Natl. Acad. Sci. USA* 97(21):11455-11459. The teachings of Schenk as applied by the examiner are discussed above in the §102(b) rejection. The examiner applies Frenkel et al. for its teaching of an

immunization procedure for the production of anti-aggregating β-amyloid antibodies based on filamentous phages displaying a particular epitope of β-amyloid and takes the position that it would have been obvious to one of ordinary skill in the art at the time the invention was made to select a filamentous bacteriophage as taught by Frenkel et al. for displaying APP fragments disclosed by Schenk as the specific viral display vehicle for an immunizing composition. This rejection is respectfully traversed.

Frenkel only teaches β-amyloid epitopes and does not provide any suggestion or motivation to induce an immune response against the β-secretase cleavage site or to use an epitope spanning the β-secretase cleavage site to raise such an immune response. Thus, Frenkel cannot satisfy the deficiencies noted in Schenk as discussed above in the anticipation rejection. There is certainly no teaching, suggestion or motivation in either Schenk or Frenkel that would lead one of ordinary skill in the art to arrive at the presently claimed invention.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting

their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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